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Proposed Registration Document PRD2014-09

Cydia pomonella Granulovirus strain M

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Overview

Proposed Registration Decision for *Cydia pomonella* Granulovirus strain M

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of CYD-X Technical and CYD-X Insecticidal Virus, containing the biological active ingredient *Cydia pomonella* Granulovirus strain M, for the control of codling moth in apples.

CYD-X Technical (Registration Number 30119) and CYD-X Insecticidal Virus (Registration Number 30120) are conditionally registered in Canada. The detailed review for CYD-X Technical and CYD-X Insecticidal Virus can be found in Evaluation Report ERC2013-01, *Cydia pomonella* Granulovirus strain M. The current applications were submitted to convert CYD-X Technical and CYD-X Insecticidal Virus from conditional registration to full registration.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of CYD-X Technical and CYD-X Insecticidal Virus.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; and (c) health, safety and environmental benefits and social and economic impact."

more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

Before making a final registration decision on *Cydia pomonella* Granulovirus strain M, the PMRA will consider all comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision[4] on *Cydia pomonella* Granulovirus strain M, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

What Is *Cydia pomonella* Granulovirus strain M?

Cydia pomonella Granulovirus strain M is a naturally occurring baculovirus that is used as a microbial pest control agent for the control of codling moth (*Cydia pomonella*) larvae on apple trees. *Cydia pomonella* Granulovirus strain M must be ingested by codling moth larvae to become infected with the virus. Upon ingestion, the viral occlusion bodies dissolve in the larvae midgut and release infectious virions. The virions then enter the cell that line the digestive tract and replicate in the nuclei of these cells. The resulting replicated virions rapidly spread the infection to the other organs within the larva. Within a few days after ingestion of CYD-X Insecticidal Virus, the infected larva stops feeding, becomes sluggish and discoloured and eventually dies from a massive viral infection. After death, the larvae disintegrate, releasing new occlusion bodies that may infect other codling moth larvae upon ingestion. Exposed codling moth larvae die within three to seven days after ingestion of CYD-X Insecticidal Virus, depending on dosage and ambient temperature. Codling moth death may occur more quickly at higher temperatures and higher dosages. Some damage to the fruit may occur before the larvae die.

Health Considerations

Can Approved Uses of *Cydia pomonella* Granulovirus strain M Affect Human Health?

Cydia pomonella Granulovirus strain M is unlikely to affect your health when used according to label directions.

People can be exposed to *Cydia pomonella* Granulovirus strain M when handling and applying CYD-X Insecticidal Virus and when consuming treated produce.

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3 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

4 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

When assessing health risks, several key factors are considered such as:

- the microorganism's biological properties (for example, production of toxic by-products);
- reports of any adverse incidents;
- its potential to cause disease or toxicity as determined in toxicological studies; and
- the levels to which people may be exposed relative to exposures already encountered in nature to other isolates of this microorganism.

Toxicological studies in laboratory animals describe potential health effects from large doses in order to identify any potential pathogenicity, infectivity and toxicity concerns. Because of the close relationships within the family Baculoviridae, results and findings from studies with various other baculoviruses are considered applicable to *Cydia pomonella* Granulovirus strain M and may be used for risk assessment purposes.

Studies in the published literature examining the effects of the exposure of various baculoviruses to laboratory animals yielded no signs of toxicity, disease or irritation. No member of this family of viruses is known to infect vertebrate animals. Furthermore, baculoviruses are highly host specific and have only been found in arthropods. The presence of insect debris in CYD-X Insecticidal Virus, however, may cause irritation if inhaled or exposed to the skin or eye. Finally, baculoviruses are commonly found in nature at relatively high levels.

The use of CYD-X Insecticidal Virus is not expected to significantly increase the baculovirus level in the environment. Baculoviruses have also been used for biological insect control for over 100 years. There have been no adverse effects noted as a result of either natural populations of baculoviruses or to applications of baculovirus-based pesticides.

As is the case with all microbial pest control agents, *Cydia pomonella* Granulovirus strain M contains substances that can cause allergic reactions in people who are repeatedly exposed to it at high concentrations. However, these reactions can be avoided if farm workers and applicators follow label recommendations to minimize or limit exposure to CYD-X Insecticidal Virus.

Occupational Risks from Handling CYD-X Insecticidal Virus

Occupational risks are not of concern when CYD-X Insecticidal Virus is used according to the proposed label directions, which include protective measures.

Workers using CYD-X Insecticidal Virus can come into direct contact with *Cydia pomonella* Granulovirus strain M (that is, through contact with skin or eyes, or by inhalation). Although the potential for toxicity is low in individuals exposed to *Cydia pomonella* Granulovirus strain M, the presence of insect debris in the end-use product may cause irritation if inhaled or exposed to the skin or eyes. Sensitization may also occur upon repeated exposure to high concentrations of the product. For this reason, users must wear a long-sleeved shirt, long pants, shoes plus socks, water-proof gloves, eye goggles and a dust/mist filtering respirator (MSH/NIOSH approval number prefix TC-21C) or a NIOSH approved respirator with any N-95, R-95, P-95 or HE filter for biological products while handling, mixing/loading or applying the product and during all clean-up/repair activities.

For bystanders, exposure is expected to be much less than that of workers involved in loading and application activities and is considered negligible. Therefore, health risks to bystanders are not of concern.

Residues in Water and Food

Dietary risks from food and water are not of concern.

As part of the assessment process prior to the registration of a pesticide, Health Canada must determine whether the consumption of the maximum amount of residues, that are expected to remain on food products when a pesticide is used according to label directions, will not be a concern to human health. This maximum amount of residues expected is then legally established as a maximum residue limit under the *Pest Control Products Act* for the purposes of the adulteration provision of the *Food and Drugs Act*. Health Canada sets science-based maximum residue limits to ensure the food Canadians eat is safe.

Although isolates of *Cydia pomonella* Granulovirus are common in nature, the residues of *C. pomonella* Granulovirus strain M remaining on produce from the use of CYD-X Insecticidal Virus are expected to be higher than levels naturally occurring on fruit; however, studies in the published literature on other baculoviruses have demonstrated a lack of toxicity when laboratory animals were exposed via the oral route. Similarly, no signs of infectivity were observed in tissue culture testing.

Furthermore, the mode of action associated with baculoviruses is not dependent on toxin production. Therefore, dietary risks are minimal to non-existent and the establishment of a maximum residue limit is not required for *Cydia pomonella* Granulovirus strain M.

The likelihood of residues contaminating drinking water supplies is minimal. Consequently, dietary risks are also minimal.

Environmental Considerations

What Happens When *Cydia pomonella* Granulovirus strain M is Introduced Into the Environment?

Environmental risks are not of concern.

Cydia pomonella Granulovirus strain M is a natural baculovirus isolate that infects and kills the larval life stage of codling moth insects. Baculoviruses are generally specific to certain insect species. No member of the Baculoviridae family is known to infect vertebrates or plants. Granuloviruses have only been reported from members of the order Lepidoptera (moths and butterflies). Infectivity of Granuloviruses is limited to insect species within the same family as the host from which it was originally isolated (codling moth; *C. pomonella*). In the case of *Cydia pomonella* Granulovirus strain M, infectivity is limited to the family Tortricidae. Effects on even more distantly-related non-target organisms are, therefore, not expected.

Furthermore, baculoviruses are ubiquitous in the environment. The use of CYD-X Insecticidal Virus to control codling moth in apple orchards is not expected to significantly increase the baculovirus load in the environment beyond naturally-occurring levels. Baculoviruses, including other strains of *Cydia pomonella* Granulovirus, have been extensively used as biological control agents. No reports of adverse effects have been noted on non-target organisms due to either natural population of baculoviruses or to applications of baculovirus-based pesticide products.

Value Considerations

What Is the Value of CYD-X Insecticidal Virus?

CYD-X Insecticidal Virus has value in controlling codling moth, which is a major pest of apples; it can be used by organic growers and in integrated pest management programs.

The crop and pest combination of apples and codling moth has been identified in the Grower Priority Database as a high priority and is present on the labels of three active ingredients (azinphos-methyl, diazinon and endosulfan) which are being phased out for use in Canada. *Cydia pomonella* Granulovirus strain M can be used by organic growers and is another tool that be utilized in codling moth integrated pest management programs.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures on the label of CYD-X Insecticidal Virus to address the potential risks identified in this assessment are as follows:

Key Risk-Reduction Measures

Human Health

Statements warning users that the product is a dermal and eye irritant, as well as a potential sensitizer, are required on the label.

To minimize exposure to mists generated while handling, mixing/loading or applying the product and during all clean-up/repair activities, users must wear a long-sleeved shirt, long pants, shoes plus socks, water-proof gloves, eye goggles and a dust/mist filtering respirator (MSH/NIOSH approval number prefix TC-21C) or a NIOSH approved respirator with any N-95, R-95, P-95 or HE filter for biological products.

Environment

As a general precaution, to reduce runoff, users must not apply the product to aquatic systems and contamination of irrigation or drinking water supplies and aquatic habitats is prohibited. Furthermore, users are directed to not apply the product by air and to follow application instructions to minimize spray drift. Standard disposal statements for unused or unwanted product and the product container also apply.

Next Steps

Before making a final registration decision on *Cydia pomonella* Granulovirus strain M, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

Other Information

When the PMRA makes its registration decision, it will publish a Registration Decision on *Cydia pomonella* Granulovirus strain M (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

Cydia pomonella Granulovirus strain M

1.0 The Active Ingredient, Its Properties and Uses

CYD-X Technical contains > 6×10^{13} occlusion bodies (OB)/L (equivalent to 0.12% weight-by-weight [w/w]) and CYD-X Insecticidal Virus > 3×10^{13} OB/L (equivalent to 0.06% w/w). The chemistry databases for CYD-X Technical and CYD-X Insecticidal Virus are complete.

For more details on the identity of the active ingredient and the physical and chemical properties of the active ingredient and end-use product, please refer to Evaluation Report ERC2013-01, *Cydia pomonella* Granulovirus strain M.

1.1 Directions for Use

CYD-X Insecticidal Virus is for use in apples to control codling moth larvae. This product is to be applied at a rate of 250 mL per hectare in sufficient water for thorough coverage of the tree canopy. Application timing is against small larvae just after egg hatch and prior to entering the fruit; early in the spring for the first generation and later in the summer for the second generation.

1.2 Mode of Action

Cydia pomonella Granulovirus strain M must be ingested by codling moth larvae to become infected with the virus. Upon ingestion, the viral occlusion bodies dissolve in the larvae midgut and release infectious virions. The virions then enter the cell that line the digestive tract and replicate in the nuclei of these cells. The resulting replicated virions rapidly spread the infection to the other organs within the larva. Within a few days after ingestion of CYD-X Insecticidal Virus, the infected larva stops feeding, becomes sluggish and discoloured and eventually dies from a massive viral infection. After death, the larvae disintegrate, releasing new occlusion bodies that may infect other codling moth larvae upon ingestion. Exposed codling moth larvae die within 3 to 7 days after ingestion of CYD-X Insecticidal Virus, depending on dosage and ambient temperature. Codling moth death may occur more quickly at higher temperatures and higher dosages.

2.0 Methods of Analysis

CYD-X Technical contains > 6×10^{13} OB/L (equivalent to 0.12% w/w) and CYD-X Insecticidal Virus > 3×10^{13} OB/L (equivalent to 0.06% w/w). The information provided in response to the Section 12 notice confirms acceptable protocols were used to determine that the microbial contamination in CYD-X Insecticidal Virus meets the PMRA requirements. The current label storage statements for CYD-X Insecticidal Virus were supported by the submitted storage stability data. The results of the REN analysis confirm this is an acceptable method for distinguishing the MPCA from other strains of *Cydia pomonella* Granulovirus. This new information does not impact upon the previous human health and environmental assessments published in Evaluation Report ERC2013-01, *Cydia pomonella* Granulovirus strain M. The chemistry databases for CYD-X Technical and CYD-X Insecticidal Virus are complete.

For more details on Methods of Analysis, please refer to ERC2013-01.

3.0 Impact on Human and Animal Health, Environment, and Value

Please refer to ERC2013-01.

4.0 Pest Control Product Policy Considerations

Please refer to ERC2013-01.

5.0 Summary

Methods for Analysis of the Microorganism as Manufactured

The product characterization data for CYD-X Technical and CYD-X Insecticidal Virus are adequate to assess their potential human health and environmental risks. The technical grade active ingredient was characterized and the specifications were supported by the analyses of a sufficient number of batches to permit a registration decision.

CYD-X Technical contains > 6×10^{13} OB/L (equivalent to 0.12% w/w) and CYD-X Insecticidal Virus > 3×10^{13} OB/L (equivalent to 0.06% w/w). The information provided in response to the Section 12 notice confirms acceptable protocols were used to determine that the microbial contamination in CYD-X Insecticidal Virus meets the PMRA requirements. The current label storage statements for CYD-X Insecticidal Virus were supported by the submitted storage stability data. The results of the REN analysis confirm this is an acceptable method for distinguishing the microbial pest control product from other strains of *Cydia pomonella* Granulovirus. This new information does not impact upon the previous human health and environmental assessments published in Evaluation Report ERC2013-01, *Cydia pomonella* Granulovirus strain M. The chemistry databases for CYD-X Technical and CYD-X Insecticidal Virus are complete.

For the summary of human health and safety, environmental risks, and value, please refer to ERC2013-01.

6.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of CYD-X Technical and CYD-X Insecticidal Virus, containing the technical grade active ingredient *Cydia pomonella* Granulovirus strain M, to control codling moth (*Cydia pomonella*) larvae on apple trees.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

List of Abbreviations

ERC	Evaluation Report
L	litre
OB	occlusion bodies
PMRA	Pest Management Regulatory Agency
w/w	weight by weight basis

References

PMRA Document Number	Reference
2069660	2011, Comparative Restriction Analysis of CpGV (CYD-X), DACO: M2.7.1 CBI
2346401	Storage Stability Testing, DACO: M2.11 CBI
2346395	Unintentional Ingredients, DACO: M2.9.3 CBI
2346396	USP 35 Method 62 - Microbial Examination of Non-sterile Products: Tests for Specified Microorganisms, DACO: M2.10.2 CBI
2346397	AOAC Official Method 991.14 Coliform and Escherichia coli Counts in Foods, DACO: M2.10.2 CBI
2346398	Enumeration of Enterococci, DACO: M2.10.2 CBI